
Molecular characterization of the transition from acute to chronic kidney injury following ischemia/reperfusion.

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Authors: Jing Liu, Sanjeev Kumar, Egor Dolzhenko, Gregory F Alvarado, Jinjin Guo, Can Lu, Yibu Chen, Meng Li, Mark C Dessing, Riana K Parvez, Pietro E Cippa, A Michaela Krautzberger, Gohar Saribekyan, Andrew D Smith, Andrew P McMahon

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Scientific Abstract:

Though an acute kidney injury (AKI) episode is associated with an increased risk of chronic kidney disease (CKD), the mechanisms determining the transition from acute to irreversible chronic injury are not well understood. To extend our understanding of renal repair, and its limits, we performed a detailed molecular characterization of a murine ischemia/reperfusion injury (IRI) model for 12 months after injury. Together, the data comprising RNA-sequencing (RNA-seq) analysis at multiple time points, histological studies, and molecular and cellular characterization of targeted gene activity provide a comprehensive profile of injury, repair, and long-term maladaptive responses following IRI. Tubular atrophy, interstitial fibrosis, inflammation, and development of multiple renal cysts were major long-term outcomes of IRI. Progressive proximal tubular injury tracks with de novo activation of multiple Krt genes, including Krt20, a biomarker of renal tubule injury. RNA-seq analysis highlights a cascade of temporal-specific gene expression patterns related to tubular injury/repair, fibrosis, and innate and adaptive immunity. Intersection of these data with human kidney transplant expression profiles identified overlapping gene expression signatures correlating with different stages of the murine IRI response. The comprehensive characterization of incomplete recovery after ischemic AKI provides a valuable resource for determining the underlying pathophysiology of human CKD.

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